



recommendations and should permit the OTC marketing of these combination oral health care products in accordance with the Subcommittee's proposed monograph.

#### **4 Recommendations for Revisions to the Labeling of OTC Antigingivitis and Antigingivitis/Antiplaque Drug Products**

##### **Task Group Position and Recommendations**

The Task Group has reviewed the proposed labeling and believes it would be in the best interest of consumers to modify the proposed indications and warnings. The **indications** sections should be revised so that the labeling is consistent for all products and broadened to allow multiple descriptions of drug effects. The addition of a few words to the regulation for technical clarification will achieve this goal.

The **warnings** in the Subcommittee's report should be revised to be more consistent with longstanding FDA policy on warnings. As the warnings are currently proposed to be worded, the language could mislead consumers by not conveying appropriate use information. It is important that consumers understand that they should ask their dentist if their condition worsens or does not improve after regular use of the product. In addition, the Task Group recommends inclusion of the phrase "See your dentist regularly," in the other information section of the Drug Facts box.

##### **4.1 *The Indications and Uses Should Be Revised***

"Indications" on OTC labels are synonymous with the term "uses." Indications are differentiated from the statement of identity by location and content. Indications usually expand on the type of benefits that can be expected from the product. The Subcommittee's recommendations are very restrictive in the types of information that can be conveyed to the

consumer in the “uses” section of the Drug Facts box. The “uses” recommended by the Subcommittee for antigingivitis/antiplaque products are summarized in the following table.

<b>The Subcommittee Recommended Uses</b>			
<b>356.65 (b)(1): For all antigingivitis products.</b>	<b>356.65 (b)(2): For antigingivitis products containing stannous fluoride.</b>	<b>356.65 (b)(3): For all antigingivitis/antiplaque products.</b>	<b>356.66 (b)(10): For fixed combination of essential oils</b>
helps [select one of the following]: <ul style="list-style-type: none"> <li>• control</li> <li>• <u>reduce</u></li> <li>• prevent</li> </ul>	356.65(b)(1) and/or <ul style="list-style-type: none"> <li>• helps interfere with harmful effects of plaque associated with gingivitis.</li> </ul>	helps [select one of the following] <ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> <li>• remove</li> </ul>	one or more of the indications for antigingivitis/antiplaque active ingredients in 356.65(b)(3), or the following: <ul style="list-style-type: none"> <li>• helps [select one of the following]:  <ul style="list-style-type: none"> <li>• control</li> <li>• inhibit</li> <li>• kill</li> </ul> </li> </ul>
[select one or more of the following]: <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>		plaque that leads to [select one or more of the following]: <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>	plaque bacteria that contribute to the development of [select one or more of the following]: <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>

#### 4.1.1 Indications and Uses Should be Broadened to Allow Multiple Descriptions of Drug Effects for Gingivitis

The ANPR recommended that only one of three words -- “control,” “reduce,” or “prevent” -- be permitted to describe the action of antigingivitis/ antiplaque products on “gingivitis” or “gingivitis, an early form of gum disease” or “bleeding gums.” Not only is this recommendation unnecessarily restrictive in the information that could be conveyed to the consumer in the “uses” section of Drug Facts, it is unreasonable because the terms “control,” “reduce,” or “prevent” are not mutually exclusive. For example, a consumer with mild

gingivitis could purchase a product to control or reduce gingivitis and continue to use the same product to prevent future gingivitis. A product that can both reduce and prevent gingivitis should be labeled for both indications. In addition, restriction to one term ("control," "reduce," or "prevent") is not meaningful to consumers who want to control, reduce or prevent their existing gingivitis and also prevent gingivitis in additional areas.

The Task Group recommends that antigingivitis (356.65 (b)(1)), stannous fluoride (356.65 (b)(2)), antigingivitis and antiplaque (356.65 (b)(3)) and the fixed combination of essential oils products (356.66(b)(10)) be permitted to use one *or more* of the statements for gingivitis: "control," "reduce," "prevent." These statements provide consumers with truthful information about a product's uses, especially if the consumer uses the product for more than one purpose. The Task Group's recommended changes (bolded) for the gingivitis portion of the indication are as follows:

<b>Task Group Recommended Uses for Gingivitis</b>			
<b>356.65 (b)(1): For all antigingivitis products</b>	<b>356.65 (b)(2): For antigingivitis products containing stannous fluoride.</b>	<b>356.65 (b)(3): For all antigingivitis/antiplaque products.</b>	<b>356.66(b)(10): For fixed combination of essential oils</b>
helps [select one <u>or more</u> of the following]	helps [select one <u>or more</u> of the following]	helps [select one <u>or more</u> of the following]	helps [select one <u>or more</u> of the following]
<ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul>	<ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul>	<ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul>	<ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul>
[select one or more of the following]	[select one or more of the following]	[select one or more of the following]	[select one or more of the following]
<ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>	<ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>	<ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>	<ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>

#### **4.1.2 Provision for the Effect of Antigingivitis and Antiplaque Agents on Plaque Should Be Broadened to Allow Multiple Descriptions of Drug Effects**

For all products effective in reducing gingivitis and plaque (356.65 (b)(3)) the Subcommittee recommended an indication that the product helps "control," "reduce," "prevent" or "remove" plaque that leads to "gingivitis," "gingivitis, an early form of gum disease;" and/or "bleeding gums." Thus, an example of the uses or indications of a product containing an antigingivitis and antiplaque ingredient would read, "Helps reduce plaque that leads to gingivitis." Such an indication/use only communicates a portion of the capabilities of the active ingredients. Ingredients that have been categorized both as antigingivitis and antiplaque have demonstrated effectiveness for both antigingivitis and antiplaque clinical endpoints.

Limiting these products to declaring the benefits of "controlling," "reducing," "preventing," or "removing" plaque that leads to gingivitis fails to communicate established product benefits for these products on gingivitis. Ingredients classified as antigingivitis/antiplaque have demonstrated effectiveness in reducing plaque and reducing gingivitis in subjects with pre-existing gingivitis. This was confirmed by the Subcommittee and these benefits should be permitted to be communicated to consumers.

The Task Group recommends that the labeling in proposed section 356.65 (b)(3) be broadened to include both the antigingivitis and antiplaque benefits of these ingredients. This also applies to the labeling in section 356.65 (b)(2) in that stannous fluoride also showed a benefit for both antigingivitis and the "harmful effects of plaque." Thus, the indications/uses for all antigingivitis/antiplaque and stannous fluoride products should be revised to show the benefits for gingivitis and plaque as follows:

<b>Task Group Recommended Uses for Plaque</b>	
<b>356.65 (b)(2): For antigingivitis products containing stannous fluoride</b>	<b>356.65 (b)(3): For all antigingivitis/antiplaque products.</b>
<p>helps [select <u>one or more</u> of the following]:</p> <ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul> <p>[select one or more of the following]:</p> <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul> <p>and (optionally)</p>	<p>helps [select <u>one or more</u> of the following]:</p> <ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> </ul> <p>[select one or more of the following]:</p> <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul> <p>and (optionally)</p>
<p>helps interfere with the harmful effects of <u>plaque or</u> plaque that leads to [select one or more of the following]:</p> <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>	<p>helps [select one or more of the following]:</p> <ul style="list-style-type: none"> <li>• control</li> <li>• reduce</li> <li>• prevent</li> <li>• remove</li> </ul> <p><u>plaque or</u> plaque that leads to [select one or more of the following]:</p> <ul style="list-style-type: none"> <li>• gingivitis</li> <li>• gingivitis, an early form of gum disease</li> <li>• bleeding gums</li> </ul>

#### 4.1.3 Indications for the Killing of Plaque Bacteria and Antiplaque/Antigingivitis Claims for Fixed Combination of Essential Oils Products Should Not Be Mutually Exclusive

Additional indications relating to the killing of plaque bacteria and antiplaque/antigingivitis claims for the fixed combination of essential oils products should not be mutually exclusive. Proposed Section 356.66(b)(10) does not reflect this point. The fixed combination of essential oils products identified in section 356.26 should be permitted to use the indication in Section 356.65(b)(1), Section 356.65(b)(3) and *optionally* the language in Section 356.66(b)(10).

#### 4.1.4 Summary of Recommendations For Labeling "Uses"

Section 356.65(b)(1) should be the basic monograph indication for all antigingivitis products. Antiplaque/antigingivitis ingredients covered under section 356.65(b)(3) could use the indication in section 356.65(b)(1) or the additional language in section 356.65 (b)(3). Stannous fluoride covered under section 356.65(b)(2) could use the indication in section 356.65(b)(1) or the additional language section 356.65(b)(2). The fixed combination of essential oils identified in section 356.26(b) could use the indication in section 356.65(b)(1), section 356.65(b)(3), and optionally the language in section 356.66(b)(10). These recommendations are added to the proposed regulations below. Additions are bolded, italicized, and underlined.

(b) Indications. The labeling of the product states, under the heading "Uses," one or more of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this part, may also be used, as provided in Sec. 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) For all antigingivitis ***and all antiplaque/antigingivitis*** products. The labeling states "[bullet] helps [select one ***or more*** of the following: 'control,' 'reduce,' or 'prevent'] [select one or more of the following: '[bullet] gingivitis,' '[bullet] gingivitis, an early form of gum disease,' or '[bullet] bleeding gums']."

(2) For antigingivitis products containing stannous fluoride. The labeling states the indication in paragraph (b)(1) of this section and/or the following: "helps ***interfere with harmful effects of plaque***" or "helps interfere with harmful effects of plaque associated with [select one ***or more*** of the following: '[bullet] gingivitis,' ***'[bullet] gingivitis, an early form of gum disease,' or '[bullet] bleeding gums'.***"

(3) For all antigingivitis/antiplaque products. ***The labeling states the indication in paragraph (b)(1) of this section and/or the following:*** and

optionally “[bullet] helps [select one **or more** of the following: ‘control,’ ‘reduce,’ ‘prevent,’ or ‘remove’] plaque **or plaque** that leads to [select one or more of the following: ‘[bullet] gingivitis,’ ‘[bullet] gingivitis, an early form of gum disease,’ or ‘[bullet] bleeding gums’].”

**Sec. 356.66 Labeling of combination drug products.**

(b) \* \* \*

(10) For permitted combinations identified in Sec. 356.26(p). The labeling of the product states, under the heading “Uses,” one or more of the indications for antigingivitis/antiplaque active ingredients in Sec. 356.65(b)(3), **and optionally** the following: “[bullet] helps [select one **or more** of the following: ‘control,’ ‘inhibit,’ or ‘kill’] plaque bacteria that contribute to the development of [select one or more of the following: ‘[bullet] gingivitis,’ ‘[bullet] gingivitis, an early form of gum disease,’ or ‘[bullet] bleeding gums’].”

In summary, the Task Group recommends that FDA revise the indications/uses section to read as below. Additions are bolded, underlined, and italicized.



## Summary of Task Group Recommendations for Labeling "Uses"

356.65 (b)(1) For all antigingivitis products	356.65(b)(2) For antigingivitis products containing stannous fluoride	356.65(b)(3) For all antigingivitis/antiplaque products	356.65(b)(10) For permitted combinations
<p>helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> </ul> <p>[Select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li>gingivitis, an early form of gum disease</li> <li>bleeding gums</li> </ul>	<p>helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> </ul> <p>[Select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li>gingivitis, an early form of gum disease</li> <li>bleeding gums</li> </ul>	<p>helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> </ul> <p>[Select one or more of the following]</p> <ul style="list-style-type: none"> <li><u>gingivitis</u></li> <li><u>gingivitis, an early form of gum disease</u></li> <li><u>bleeding gums</u></li> </ul>	<p>helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> </ul> <p>[Select one or more of the following]</p> <ul style="list-style-type: none"> <li><u>gingivitis</u></li> <li><u>gingivitis, an early form of gum disease</u></li> <li><u>bleeding gums</u></li> </ul>
	<p style="text-align: center;">AND/OR</p> <div> <div><u>helps interfere with harmful effects of plaque</u></div> <div>OR</div> <div> <p>helps interfere with harmful effects of plaque associated with</p> <p>[Select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li><u>gingivitis, an early form of gum disease</u></li> <li><u>bleeding gums</u></li> </ul> </div> </div>	<p style="text-align: center;">AND (OPTIONALLY)</p> <div> <div><u>helps</u></div> <div>OR</div> <div> <p>Helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> <li>remove</li> </ul> <p>plaque that leads to</p> <p>[select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li>gingivitis, an early form of gum disease</li> <li>bleeding gums</li> </ul> </div> </div>	<p style="text-align: center;">AND (OPTIONALLY)</p> <div> <div><u>helps</u></div> <div>OR</div> <div> <p>Helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>reduce</li> <li>prevent</li> <li>remove</li> </ul> <p>plaque that leads to</p> <p>[select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li>gingivitis, an early form of gum disease</li> <li>bleeding gums</li> </ul> </div> </div>
			<p style="text-align: center;">AND (OPTIONALLY)</p> <div> <div><u>helps</u></div> <div>OR</div> <div> <p>helps [select one <u>or more</u> of the following]</p> <ul style="list-style-type: none"> <li>control</li> <li>inhibit</li> <li>kill</li> </ul> <p><u>plaque bacteria</u></p> <p>plaque bacteria that contribute to the development of</p> <p>[select one or more of the following]</p> <ul style="list-style-type: none"> <li>gingivitis</li> <li>gingivitis, an early form of gum disease</li> <li>bleeding gums</li> </ul> </div> </div>

\* Task Group recommended changes are underlined, bolded and italicized